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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/012,194	12/06/2001	Manuela Martins-Green	407E-914500US	5287

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EXAMINER	
QIAN, CELINE X	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 12/31/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/012,194	MARTINS-GREEN ET AL.	
	Examiner	Art Unit	
	Celine X Qian	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32 and 34-42* is/are pending in the application.

4a) Of the above claim(s) *21,22,24,27-32 and 34-42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20,23,25 and 26* is/are rejected.

7)☒ Claim(s) *23* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 1-32 and 34-42 are pending in the application.

Election/Restrictions

Applicant's election with traverse of Group I in the response filed on 10/2/03 is acknowledged. The traversal is on the ground(s) that a search of both Groups I and II would not pose a serious burden. Applicants argue that a search of the artificial tissue of Group I would also identify the art that is relevant to the method of making said tissue (Group II). Applicants further argue that since the artificial tissue made by the method of Group II is placed with invention of Group I, therefore, Group I and II should be combined. This is not found persuasive. The invention of Groups I and II are patentably distinct for reasons set forth of the record mailed on 8/26/03. The artificial of Group I can be made by methods other than the method claimed in Group II. A search of the invention of Group I is not co-extensive with a search of the invention of Group II. Therefore, it would be burdensome to search both Group I and II in a single application.

The requirement is still deemed proper and is therefore made FINAL.

Accordingly, claims 21, 22, 24, 27-32, 34-42 are withdrawn from consideration for being directed to non-elected subject matter. Claims 1-20, 23, 25 and 26 are currently under examination.

Drawings

Appendix A and B contain drawings that do not comply with the drawing requirement. Applicants need to remove the legends from the drawing and place such description in the specification (brief description of the drawing section).

Claim Objections

Claim 23 is objected to for depending on non-elected base claims (21 and 22).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6, 8-20, 23, 25 and 26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an artificial tissue comprising a support matrix, microvascular endothelial cells from a first animal, and connective tissue from a second animal, and/or epithelial cells from a third animal, wherein the artificial tissue comprises one or more microvessels produce therein, wherein the first, second and third animal are same, does not reasonably provide enablement for such an artificial tissue wherein the first, second and third animal are different. Further, the specification fails to enable such an artificial tissue, wherein the microvessel produces blood cell. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/use the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to: (a) the nature of the invention; (b) the breadth of the claims; (c) the state of the prior art; (d) the amount of direction provided by the inventor; (e) the existence of working examples; (f) the relative skill of those in the art; (g) whether the quantity of experimentation needed to

make or use the invention based on the content of the disclosure is "undue"; and (h) the level of predictability in the art (MPEP 2164.01 (a)).

The nature of the invention is an artificial tissue comprising a support matrix, microvascular endothelial cells from a first animal, and connective tissue from a second animal, and/or epithelial cells from a third animal, wherein the artificial tissue comprises one or more microvessels produce therein.

The breadth of the claims is broad. The broadest claim is drawn to an artificial tissue comprising a support matrix, microvascular endothelial cells from a first animal, and connective tissue from a second animal, and/or epithelial cells from a third animal, whereby each of the component are isolated from animals of either different species or different origin. The claims are further drawn to such an artificial tissue which produces blood cells.

The teaching of the specification is limited. The specification teaches the generation of an artificial skin model by culturing human primary skin karytinocytes on top of human primary lung microvascular cells (hMVEC) supported by collagen matrix. The specification teaches that such artificial tissue can be used in studying tissue development and repair, tissue replacement and grafting. However, the specification fails to disclose such an artificial skin model that is made by cells from different species of the animals, and may be used for the disclosed uses. The specification also fails to teach an artificial tissue that produces blood cells *in vitro*. As such, one skilled in the art would have to rely on the teaching of the art to make and use the invention in commensurate with the scope of the claims.

The state of art at the time of filing teaches a number of criteria for in vitro reconstructed skin models for wound coverage in deep burns. Berthod et al. indicate one of such criteria is that

such artificial skin must be safe in terms of microorganism transmission and should not provoke strong immunological reactions (see page 809, 2nd col., first paragraph). The claimed invention encompasses an artificial skin made from cells isolated from different species of any type of animals. Such artificial skin would inevitably elicit strong immunological response upon graft to a host because of the immuno-rejection across species or even within a species. In addition, in an *in vitro* model of studying biological process, whether a test compound effective in one species would produce the same effect in another is unpredictable.

The state of art at the time of filing teaches that hematopoietic stem cells are ultimately responsible for the constant renewal of blood *in vivo* (see Stem cells, page 43). Such hematopoietic stem cells are found in adult bone marrow, peripheral blood and umbilical cord blood (see Stem cells, page 46). The claimed artificial tissues does not comprise cells of hematopoietic origin. In addition, the specification fails to demonstrate that the artificial skin can produce blood cells in an *in vitro* setting. Therefore, whether the microvessels produce in the claimed artificial tissue can produce blood cells is unpredictable.

In view of the limited teaching of the specification, one skilled in the art would have to engage in undue experimentation to make/use the invention in commensurate with the scope of the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 6, 7, 9, 11, 12, 15, 18, 19, 20, 25 and 26 are rejected under 35 U.S.C. 102(b) as being anticipated by Black et al (1998, FASEB J. 12, 1331-1340).

Black et al. disclose a skin equivalent preparation comprising human keratinocytes plated on endothelial dermal equivalent or endothelial fibroblast dermal equivalent (see page 1333, 1st col., 2nd and 3rd paragraph). Black et al. also disclose that the endothelial fibroblast dermal equivalent comprising fibroblast and HUVEC (see page 1333, 1st col., 2nd paragraph). Black et al. further disclose that a network of capillary-like tubular structures is formed in the tissue (see page 1333, 2nd col., 3rd and 5th paragraph). Black et al. disclose that said tissue produces laminin, type IV collagen and extracellular matrix (see page 1334, 1st col., 2nd paragraph, and Figures 1, 2 and 3). Moreover, Black et al. disclose that said tissue is self maintained in vitro, and is suitable for tissue graft (see page 1338, entire 1st col., and 2nd col., 2nd paragraph). Therefore, Black et al. disclose the instantly claimed invention.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X Qian whose telephone number is 703-306-0283. The examiner can normally be reached on 9:00-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel Ph.D. can be reached on 703-305-1998. The fax phone number for the organization where this application or proceeding is assigned is 703-305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Anne-marie Falk

ANNE-MARIE FALK, PH.D
PRIMARY EXAMINER

Celine Qian, Ph.D.